FILE 'CAPLUS' ENTERED AT 15:10:35 ON 29 SEP 2001

L1 175 SEA CETRORELIX

L2 5 SEA L1 AND LYOPHILIZ?

D L2 1-5, TI, KWIC

D L2 5 STD

D L2 1-5 STD, AB, KWIC

CODEN: EPXXDW
DT Patent
LA German
IC ICM A61K037-43
ICS A61K047-12
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 611572	A2	19940824	EP 1994-101672	19940204
	EP 611572	A3	19950111		
	EP 611572	B1	20000607		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	DE 4305225	A1	19940825	DE 1993-4305225	19930219
	EP 947200	A2	19991006	EP 1999-102340	19940204
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	AT 193653	E	20000615	AT 1994-101672	19940204
	ES 2148247	T3	20001016	ES 1994-101672	19940204
	CZ 284314	B6	19981014	CZ 1994-312	19940214
	CZ 285768	B6	19991117	CZ 1998-974	19940214
	AU 9455235	A1	19940825	AU 1994-55235	19940217
	AU 671881	B2	19960912		
	JP 06271476	A2	19940927	JP 1994-20532	19940217
	PL 177177	B1	19991029	PL 1994-302266	19940217
	CA 2115943	AA	19940820	CA 1994-2115943	19940218
	FI 9400779	A	19940820	FI 1994-779	19940218
	NO 9400564	A	19940822	NO 1994-564	19940218
	ZA 9401136	A	19940829	ZA 1994-1136	19940218
	BR 9400617	A	19940927	BR 1994-617	19940218
	HU 67117	A2	19950228	HU 1994-481	19940218
	HU 218281	B	20000728		
	CN 1112010	A	19951122	CN 1994-101378	19940218
	RU 2145234	C1	20000210	RU 1994-5001	19940218
PRAI	DE 1993-4305225	A	19930219		
	EP 1994-101672	A3	19940204		

=> d L2 1-5 std, ab, kwic

L2 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2001 ACS
AN 2001:73538 CAPLUS
DN 134:136699
TI Pharmaceutical formulations comprising water-insoluble complex of a peptides for sustained drug delivery
IN Gefter, Malcolm L.; Barker, Nicholas; Musso, Gary; Molineaux, Christopher J.
PA Praecis Pharmaceuticals, Inc., USA
SO U.S., 19 pp., Cont.-in-part of U.S. 5,968,895.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K038-00
NCL 514013000
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6180608	B1	20010130	US 1997-988851	19971211

CN 1245436 A 20000223 CN 1997-181608 19961211
ZA 9710994 A 19980710 ZA 1997-10994 19971208
PRAI US 1996-762747 A2 19961211
OS MARPAT 134:136699
AB Sustained delivery formulations comprising a water-insol. complex of a peptidic compd. (e.g., a peptide, polypeptide, protein, peptidomimetic or the like) and a carrier macromol. are disclosed. The formulations of the invention allow for loading of high concns. of peptidic compd. in a small vol. and for delivery of a pharmaceutically active peptidic compd. for prolonged periods, e.g., one month, after administration of the complex. The complexes of the invention can be milled or crushed to a fine powder. In powd. form, the complexes form stable aq. suspensions and dispersions, suitable for injection. In a preferred embodiment, the peptidic compd. of the complex is an LHRH analog, preferably an LHRH antagonist, and the carrier macromol. is an anionic polymer, preferably CM-cellulose. Methods of making the complexes of the invention, and methods of using LHRH-analog-contg. complexes to treat conditions treatable with an LHRH analog, are also disclosed. Thus, 50 mg of PPI-149 was dissolved in 2 mL of 5% mannitol and mixed with 2 mL of 0.5% CM-cellulose. The mixt. was stirred and immediately yielded a white ppt. The suspension was frozen and **lyophilized** to dryness to yield a PPI-149 sustained delivery complex.
RE.CNT 42
RE
(1) Anon; FR 2455459 1981 CAPLUS
(2) Anon; JP 63-310827 1988 CAPLUS
(3) Anon; WO 8805661 1988 CAPLUS
(4) Anon; EP 328090 1989 CAPLUS
(6) Anon; WO 9211844 1992 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Sustained delivery formulations comprising a water-insol. complex of a peptidic compd. (e.g., a peptide, polypeptide, protein, peptidomimetic or the like) and a carrier macromol. are disclosed. The formulations of the invention allow for loading of high concns. of peptidic compd. in a small vol. and for delivery of a pharmaceutically active peptidic compd. for prolonged periods, e.g., one month, after administration of the complex. The complexes of the invention can be milled or crushed to a fine powder. In powd. form, the complexes form stable aq. suspensions and dispersions, suitable for injection. In a preferred embodiment, the peptidic compd. of the complex is an LHRH analog, preferably an LHRH antagonist, and the carrier macromol. is an anionic polymer, preferably CM-cellulose. Methods of making the complexes of the invention, and methods of using LHRH-analog-contg. complexes to treat conditions treatable with an LHRH analog, are also disclosed. Thus, 50 mg of PPI-149 was dissolved in 2 mL of 5% mannitol and mixed with 2 mL of 0.5% CM-cellulose. The mixt. was stirred and immediately yielded a white ppt. The suspension was frozen and **lyophilized** to dryness to yield a PPI-149 sustained delivery complex.
IT 58-82-2D, Bradykinin, analogs 9000-07-1D, Carrageenan, anionic derivs. 9002-60-2, Corticotropin, biological studies 9002-64-6, Parathyroid hormone 9004-32-4 9005-32-7, Alginic acid 9005-38-3, Sodium alginate 9007-12-9, Calcitonin 9034-40-6D, LHRH, analogs 9063-38-1, Sodium starch glycolate 11000-17-2D, Vasopressin, analogs 11138-66-2, Xanthan

11141-17-6, Align 25249-06-3D, Polygalacturonic acid, anionic derivs.
71779-20-9 120287-85-6, **Cetrorelix** 183552-38-7, PPI-149
186835-68-7, PPI 258
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulations comprising water-insol. complex of peptides for sustained drug delivery)

L2 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2001 ACS
AN 2000:573692 CAPLUS
DN 133:182987
TI Sustained release salts of pharmaceutically active peptides and their production
IN Bauer, Horst; Deger, Wolfgang; Sarlikiotis, Werner; Damm, Michael
PA Asta Medica A.-G., Germany
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K047-48
ICS A61K038-09; A61K009-10; A61K009-14; A61K009-19
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000047234	A1	20000817	WO 2000-EP697	20000129
	W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRAI US 1999-119076 P 19990208
AB Substained delivery pharmaceutical compns. comprise a water insol. salt of a pharmaceutically active ionic peptide and a counterionic carrier macromol. The peptide may be an LHRH antagonist such as **cetrorelix** and the macromol. may be an anionic polysaccharide such as CM-cellulose. The salt is prepd. using ion exchangers to sep. remove the counterions from the peptide and the carrier macromol. thereby forming free peptide/macromol. ions. These free peptide and macromol. ions are then combined to form the water insol. peptide-macromol. salt. A **lyophilizate** of **cetrorelix**-CM-cellulose salt was prepd.
RE.CNT 6
RE
(1) Asta Medica Ag; WO 9842381 A 1998 CAPLUS
(2) Kamei, S; WO 9832423 A 1998 CAPLUS
(3) Klokkers-Bethke, K; US 5773032 A 1998 CAPLUS
(4) Molineaux, C; WO 9825642 A 1998 CAPLUS
(5) Nestor, J; US 4581169 A 1986 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Substained delivery pharmaceutical compns. comprise a water insol. salt of a pharmaceutically active ionic peptide and a counterionic carrier macromol. The peptide may be an LHRH antagonist such as **cetrorelix** and the macromol. may be an anionic polysaccharide such as CM-cellulose. The salt is prepd. using ion exchangers to sep. remove the counterions from the peptide and the carrier macromol. thereby forming free peptide/macromol. ions. These free peptide and macromol. ions are

then combined to form the water insol. peptide-macromol. salt. A **lyophilizate** of **cetrorelix**-CM-cellulose salt was prepd.

ST peptide drug sustained release salt; **cetrorelix** CM cellulose salt; LHRH antagonist sustained release salt

IT 120287-85-6DP, **Cetrorelix**, CM-cellulose salts
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(sustained release salts of pharmaceutically active peptides)

IT 9000-07-1D, Carrageenan, derivs. 9000-65-1, Gum tragacanth 9000-69-5, Pectin 9003-53-6D, Polystyrene, sulfated and sulfonated 9004-32-4, CM-cellulose 9005-32-7, Alginic acid 9005-38-3, Sodium alginate 9063-38-1, Sodium starch glycolate 11138-66-2, Xanthan gum 25104-18-1,
Polylysine 25249-06-3D, Polygalacturonic acid, derivs. 38000-06-5, Polylysine 120287-85-6, **Cetrorelix**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(sustained release salts of pharmaceutically active peptides)

L2 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2001 ACS
AN 1998:672495 CAPLUS
DN 129:293891
TI Immobilized activity-stabilized LHRH antagonist complexes and their production
IN Engel, Juergen; Deger, Wolfgang; Reissmann, Thomas; Losse, Guenter; Naumann, Wolfgang; Murgas, Sandra
PA Asta Medica Aktiengesellschaft, Germany
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM A61K047-48
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9842381	A1	19981001	WO 1998-EP1398	19980311
	W: AU, BR, CA, CN, CZ, HU, IL, JP, MX, NO, NZ, PL, RU, SK, TR, UA				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	DE 19712718	A1	19981001	DE 1997-19712718	19970326
	DE 19712718	C2	19990923		
	AU 9869207	A1	19981020	AU 1998-69207	19980311
	BR 9807887	A	20000222	BR 1998-7887	19980311
	EP 981377	A1	20000301	EP 1998-914877	19980311
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6022860	A	20000208	US 1998-48244	19980326
	NO 9904665	A	19990924	NO 1999-4665	19990924
	US 6054555	A	20000425	US 1999-422990	19991022
PRAI	DE 1997-19712718		19970326		
	WO 1998-EP1398		19980311		
	US 1998-48244		19980326		

AB LHRH antagonists, esp. **cetrorelix**, are complexed with suitable biophilic carriers to enable sustained, targeted release of the active substance over a period of several weeks. The acidic polyamino acids, polyaspartic and polyglutamic acids, are selected for complexation with

cetrorelix. The **cetrorelix**/polyamino acid complexes are produced from aq. solns. by combining the solns. and pptg. the complexes which are subsequently centrifuged off and vacuum dried over P2O5, preferably by **lyophilization**. These acidic polyamino acids display good sustained-release properties in a static liberation system depending on the hydrophobicity and molar mass of the polyamino acids. Animal testing demonstrated the efficacy of the **cetrorelix** /polyamino acid complexes as a depot system. By complexation of **cetrorelix** with polyamino acids, testosterone suppression can be achieved in male rats over a period of 600 h. Active substance release can thus be controlled according to polymer type and molar mass.

AB LHRH antagonists, esp. **cetrorelix**, are complexed with suitable biophilic carriers to enable sustained, targeted release of the active substance over a period of several weeks. The acidic polyamino acids, polyaspartic and polyglutamic acids, are selected for complexation with **cetrorelix**. The **cetrorelix**/polyamino acid complexes are produced from aq. solns. by combining the solns. and pptg. the complexes which are subsequently centrifuged off and vacuum dried over P2O5, preferably by **lyophilization**. These acidic polyamino acids display good sustained-release properties in a static liberation system depending on the hydrophobicity and molar mass of the polyamino acids. Animal testing demonstrated the efficacy of the **cetrorelix** /polyamino acid complexes as a depot system. By complexation of **cetrorelix** with polyamino acids, testosterone suppression can be achieved in male rats over a period of 600 h. Active substance release can thus be controlled according to polymer type and molar mass.

ST LHRH antagonist polyamino acid complex; **cetrorelix** sustained release polyaspartate polyglutamate

IT 24991-23-9D, complexes with LH-RH antagonists 25086-16-2D, complexes with LH-RH antagonists 25513-46-6D, Poly(L-glutamic acid), complexes with LH-RH antagonists 25608-40-6D, Poly(L-aspartic acid), complexes with LH-RH antagonists 26063-13-8D, Poly(L-aspartic acid), complexes with LH-RH antagonists 26655-91-4D, L-Glutamic acid/L-phenylalanine copolymer, complexes with LH-RH antagonists 31370-19-1D, L-Glutamic acid/L-leucine copolymer, complexes with LH-RH antagonists 112568-12-4D,
Antide, complexes with poly(amino acids) 120287-85-6D, **Cetrorelix**, complexes with poly(amino acids) 121850-01-9D, complexes with poly(amino acids) 124904-93-4D, Ganirelix, complexes with
poly(amino acids) 134457-26-4D, Azaline, complexes with poly(amino acids) 135215-95-1D, A-75998, complexes with poly(amino acids) 151272-78-5D, Antarelix, complexes with poly(amino acids)
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immobilized activity-stabilized LHRH antagonist complexes and their prodn.)

L2 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2001 ACS
AN 1995:677500 CAPLUS
DN 123:65874
TI Products for the application of high initial doses of **cetrorelix** and preparation of a combined package for use in treating diseases
IN Engel, Juergen; Hilgard, Peter; Reissmann, Thomas
PA Asta Medica A.-G., Germany
SO Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DT Patent

LA German
IC ICM A61K038-04
ICS A61K038-09; A61K009-00; A61K009-22; A61K009-52; A61K009-14; A61J001-00
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 657170	A1	19950614	EP 1994-118466	19941124
	EP 657170	B1	20000315		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AT 190495	E	20000415	AT 1994-118466	19941124
	ES 2145803	T3	20000716	ES 1994-118466	19941124
	CA 2137595	AA	19950610	CA 1994-2137595	19941208
	US 5663145	A	19970902	US 1994-354838	19941208
	JP 07194670	A2	19950801	JP 1994-306475	19941209
PRAI	DE 1993-4342091	A	19931209		

AB A pharmaceutical product, esp. suitable for treatment of hormone-dependent tumors, comprises a package of containers, of which .gtoreq.1 containers contain an initial dose of drug and .gtoreq.1 addnl. containers each contain a maintenance dose. The maintenance doses may be in delayed-release form. Thus, a 1-mo supply of **cetrorelix** comprised .gtoreq.1 container contg. an initial dose (1-60 mg) **lyophilized cetrorelix** acetate and .ltoreq.30 addnl. containers contg. a maintenance dose (0.1-10 mg) **lyophilized cetrorelix** acetate.

TI Products for the application of high initial doses of **cetrorelix** and preparation of a combined package for use in treating diseases

AB A pharmaceutical product, esp. suitable for treatment of hormone-dependent tumors, comprises a package of containers, of which .gtoreq.1 containers contain an initial dose of drug and .gtoreq.1 addnl. containers each contain a maintenance dose. The maintenance doses may be in delayed-release form. Thus, a 1-mo supply of **cetrorelix** comprised .gtoreq.1 container contg. an initial dose (1-60 mg) **lyophilized cetrorelix** acetate and .ltoreq.30 addnl. containers contg. a maintenance dose (0.1-10 mg) **lyophilized cetrorelix** acetate.

ST **cetrorelix** neoplasm inhibitor dosage form

IT Neoplasm inhibitors
Pharmaceutical dosage forms
(combined package for application of high initial doses of **cetrorelix** and lower maintenance doses)

IT Pharmaceutical dosage forms
(delayed-release, combined package for application of high initial doses of **cetrorelix** and lower maintenance doses)

IT Prostate gland
(disease, benign hyperplasia, combined package for application of high initial doses of **cetrorelix** and lower maintenance doses)

IT Puberty
(disorder, precocious, combined package for application of high initial doses of **cetrorelix** and lower maintenance doses)

IT Contraceptives
(male, combined package for application of high initial doses of **cetrorelix** and lower maintenance doses)

IT 9034-40-6, LH-RH

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; combined package for application of high initial doses of
cetrorelix and lower maintenance doses)

IT 120287-85-6, **Cetrorelix** 145672-81-7 145672-82-8
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined package for application of high initial doses of **cetrorelix** and lower maintenance doses)

L2 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2001 ACS
AN 1994:587330 CAPLUS
DN 121:187330
TI Preparation of a **cetrorelix lyophilized** composition
IN Engel, Juergen; Sauerbier, Dieter; Wichert, Burkhard; Reissmann, Thomas
PA Asta Medica AG, Germany
SO Eur. Pat. Appl., 5 pp.
CODEN: EPXXDW
DT Patent
LA German
IC ICM A61K037-43
ICS A61K047-12
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 611572	A2	19940824	EP 1994-101672	19940204
	EP 611572	A3	19950111		
	EP 611572	B1	20000607		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	DE 4305225	A1	19940825	DE 1993-4305225	19930219
	EP 947200	A2	19991006	EP 1999-102340	19940204
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	AT 193653	E	20000615	AT 1994-101672	19940204
	ES 2148247	T3	20001016	ES 1994-101672	19940204
	CZ 284314	B6	19981014	CZ 1994-312	19940214
	CZ 285768	B6	19991117	CZ 1998-974	19940214
	AU 9455235	A1	19940825	AU 1994-55235	19940217
	AU 671881	B2	19960912		
	JP 06271476	A2	19940927	JP 1994-20532	19940217
	PL 177177	B1	19991029	PL 1994-302266	19940217
	CA 2115943	AA	19940820	CA 1994-2115943	19940218
	FI 9400779	A	19940820	FI 1994-779	19940218
	NO 9400564	A	19940822	NO 1994-564	19940218
	ZA 9401136	A	19940829	ZA 1994-1136	19940218
	BR 9400617	A	19940927	BR 1994-617	19940218
	HU 67117	A2	19950228	HU 1994-481	19940218
	HU 218281	B	20000728		
	CN 1112019	A	19951122	CN 1994-101378	19940218
	RU 2145234	C1	20000210	RU 1994-5001	19940218
PRAI	DE 1993-4305225	A	19930219		
	EP 1994-101672	A3	19940204		

AB A **lyophilizate** of a peptide with 3-15 amino acid residues (e.g. **cetrorelix**) and .gtoreq.1 optional matrix materials (e.g. mannitol) is prepd. by dissolving in 100-10,000 wt. parts AcOH, dilg. with water, and **lyophilizing** the resulting soln. The

lyophilizate is useful for prepn. of a medication for treatment of female infertility and protection of the gonads from the follicular hyperstimulation seen with other infertility treatments.

TI Preparation of a **cetrorelix lyophilized** composition

AB A **lyophilizate** of a peptide with 3-15 amino acid residues (e.g. **cetrorelix**) and .gtoreq.1 optional matrix materials (e.g. mannitol) is prepd. by dissolving in 100-10,000 wt. parts AcOH, dilg. with water, and **lyophilizing** the resulting soln. The **lyophilizate** is useful for prepn. of a medication for treatment of female infertility and protection of the gonads from the follicular hyperstimulation seen with other infertility treatments.

ST **cetrorelix** infertility treatment **lyophilizate** prepn

IT Peptides, miscellaneous
RL: MSC (Miscellaneous)
(**lyophilization** of)

IT Freeze drying
(of **cetrorelix**, for infertility treatment)

IT Fertility
(female, disorder, treatment of, with **cetrorelix lyophilized** prepn.)

IT Pharmaceutical dosage forms
(freeze-dried, of **cetrorelix**, for infertility treatment)

IT 64-19-7, Acetic acid, uses
RL: USES (Uses)
(**cetrorelix** soln. in, for **lyophilization** for infertility treatment)

IT 69-65-8, Mannitol
RL: BIOL (Biological study)
(**lyophilization** of **cetrorelix** and, for infertility treatment)

IT 120287-85-6, **Cetrorelix**
RL: PROC (Process)
(**lyophilization** of, for infertility treatment)